

## **REMARKS**

Applicants respectfully request reconsideration of the pending claims in view of the above amendments and the following remarks.

Applicants note that a new sequence listing is being filed concurrently with this response.

Claims 39-43 have been canceled without prejudice or disclaimer. Claims 31-37, 44-49, 51-55, 57-59, 61-63, 72-76, 81-83, and 85 are currently pending. Claims 31-33, 44, 46-47, 51-52, 57-59, and 73-74 have been amended. No new matter has been inserted. Claims 31-33, 46-47, 51-52, 57-59, and 73-74 were simply amended to eliminate a redundant term. Claim 44 was simply amended to change its dependency.

## **Claim Objections**

The Examiner objected to claims 39 and 40 under 37 CFR 1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicants respectfully traverse this objection.

While not conceding the correctness of Examiner's position, in the interest of advancing prosecution, Applicants have canceled claims 39 and 40. Applicants respectfully request that this objection be withdrawn.

## **35 U.S.C. § 112, written description**

Claims 31-37, 39-49, 51-55, 57-59, 61-63, 72-76, 81-83 and 85 were rejected under 35 U.S.C. § 112, first paragraph, for written description. Applicants respectfully traverse this rejection.

The Examiner stated that the phrase "SEQ ID NO: 14" does not appear in the specification, or original claims as filed and states that this limitation is new matter. In response, Applicants point out that the specification has been amended to include the phrase "SEQ ID NO:

14 and that this limitation is not new matter because it has a basis in the specification at least at page 8 where it is stated that:

“Amino acid number designations in this application are made by reference to the sequence of Figure 3 with glutamine at position 31 designated as the first amino acid. The first 30 amino acids represent a leader sequence not present in the mature protein.”

Therefore, SEQ ID NO: 14 is supported in the specification because it is the sequence of Figure 3, (SEQ ID NO: 13) except with glutamine at position 31 designated as the first amino acid. As SEQ ID NO: 14 has explicit support in the specification, Applicants assert that it is not new matter.

The Examiner further stated that Applicant's arguments were non-persuasive because the sequence associated with SEQ ID NO: 14 was unknown. In response, Applicants point out that the specification has been amended to make the sequence associated with SEQ ID NO: 14 clear. As stated at pages 8 and 10 of the specification, SEQ ID NO: 14 is the sequence of Figure 3, (SEQ ID NO: 13) except with glutamine at position 31 designated as the first amino acid. To the extent that this rejection is still applied, the Applicants reiterate the following arguments.

The Examiner states that since no baseline sequence is provided for the “wild-type” SPE-A, none of the mutant proteins claimed meet the written description requirement. However, claims 31-37, 44, 46-47, 51-55, 57-59, 61-62, 73-74, 81-83, and 85 include SEQ ID NO's of a wild type sequence and therefore Applicants assert that the written description requirement has been met.

The Applicants also point out that according to MPEP § 2163 “there is a strong presumption that an adequate written description of the claimed invention is present when the application is filed” (emphasis added). See *In re Wertheim*, 541 F.2d 257, 263 (C.C.P.A. 1976). Possession may be shown in a variety of ways including through description of an actual

reduction to practice and describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See MPEP § 2163; *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68 (1998).

In this case, Applicants have provided both descriptions of actual reduction to practice and distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. The examples describe 9 SPE-A mutants that were made and evaluated. Four of the nine were tested for lethality, and two were determined to be nonlethal. Further, the specification specifically discloses 5 secondary structural features of this relatively small protein (220 amino acids) that are suitable locations for mutations yielding a nonlethal protein along with a functional explanation for the importance of these structural features. Therefore, the specification clearly conveys the information that the Applicant has invented the subject matter that is claimed and consequently the written description requirement has been satisfied. For at least these reasons, Applicants respectfully request that this rejection be withdrawn.

### **35 U.S.C. § 112, enablement**

Claims 31-37 were rejected under 35 U.S.C. § 112, first paragraph, for enablement. Applicants respectfully traverse this rejection.

The Examiner stated that Applicant's arguments were non-persuasive because the sequence associated with SEQ ID NO: 14 was unknown. In response, Applicants point out that the specification has been amended to make the sequence associated with SEQ ID NO: 14 clear. As stated at pages 8 and 10 of the specification, SEQ ID NO: 14 is the sequence of Figure 3, (SEQ ID NO: 13) except with glutamine at position 31 designated as the first amino acid. To the extent that this rejection is still applied, the Applicants reiterate the following arguments.

Specifically, the Examiner states that since no baseline sequence is provided for the "wild-type" SPE-A, one of skill in the art would not be able to make and use the claimed SPE-A

mutants. However, claims 31-37, 46-49, 73-76 now include SEQ ID NO's of a wild type sequence. Therefore, Applicants assert that the enablement requirement has been met. Applicants respectfully request that this rejection be withdrawn.

To the extent the Examiner maintains this rejection, Applicants point out that the MPEP, at § 2164.08, indicates that "the scope of enablement must only bear a 'reasonable correlation' to the scope of the claims." In this case, the claims relate to a mutant SPE-A toxin comprising from one to six specific mutated residues from a recited sequence. Further, the Applicants have provided a disclosure that is broadly enabling. The specification specifically discloses 5 secondary structural features of this relatively small protein (220 amino acids) that are suitable locations for mutations yielding a nonlethal protein. This extensive description of suitable regions of the protein is disclosure commensurate with the scope of claims drawn to one to six specific mutated residues. Thus, the present disclosure meets the standard for enablement as described in the MPEP at § 2164.08.

The MPEP notes that an enabling disclosure can include either specific examples or broad terminology. The present application includes working examples demonstrating the production of specific nonlethal SPE-A mutants, provides specific description of 5 secondary structural features that are suitable sites for mutations, and explicitly calls out 41 amino acids preferred as residues to be mutated, of which 6 residues are featured in the claims. Therefore, the present disclosure meets the standard for enablement as described in the MPEP at 2164.08 and in re Marzocchi.

Not only does the present application specifically identify particular regions and residues of SPE-A that are suitable for mutation, it provides working examples detailing success in producing several nonlethal SPE-A mutants. The examples describe 9 SPE-A mutants that were made and evaluated. Four of the nine were tested for lethality, and two were determined to be nonlethal. For at least these reasons, Applicants respectfully request that this rejection be withdrawn.

Claims 46, 48-49, 73, and 75-76 were separately rejected under 35 U.S.C. § 112, first paragraph, for enablement. Applicants respectfully traverse this rejection.

The Examiner stated that Applicant's arguments were non-persuasive because the sequence associated with SEQ ID NO: 14 was unknown. In response, Applicants point out that the specification has been amended to make the sequence associated with SEQ ID NO: 14 clear. As stated at pages 8 and 10 of the specification, SEQ ID NO: 14 is the sequence of Figure 3, (SEQ ID NO: 13) except with glutamine at position 31 designated as the first amino acid. To the extent that this rejection is still applied, the Applicants reiterate the following arguments.

The Examiner concedes that the specification is enabling for SPE-A vaccines designated SPE-A N20D, D45N, N20D/C98S, N20D/K157E, and N20D/D45N/C98S. However, the Examiner asserts that claims encompassing other mutants are not enabled, in part, because Applicants have not included a SEQ ID NO in the claims. In response, the Applicants point out that claims 46, 48-49, 73, and 75-76 include SEQ ID NO's. Applicants respectfully request that this rejection be withdrawn.

To the extent that the Examiner maintains this rejection, Applicants again point out that the MPEP, at § 2164.08, indicates that "the scope of enablement must only bear a 'reasonable correlation' to the scope of the claims." As the Applicants have provided numerous working examples in addition to structural information regarding suitable mutants, the standard for enablement has been met and Applicants respectfully request that this rejection be withdrawn.

Claims 47, 74 and 76 were separately rejected under 35 U.S.C. § 112, first paragraph, for enablement. Applicants respectfully traverse this rejection.

The Examiner stated that Applicant's arguments were non-persuasive because the sequence associated with SEQ ID NO: 14 was unknown. In response, Applicants point out that the specification has been amended to make the sequence associated with SEQ ID NO: 14 clear. As stated at pages 8 and 10 of the specification, SEQ ID NO: 14 is the sequence of Figure 3,

(SEQ ID NO: 13) except with glutamine at position 31 designated as the first amino acid. To the extent that this rejection is still applied, the Applicants reiterate the following arguments.

The Examiner concedes that the specification is enabling for pharmaceutical compositions comprising mutant SPE-A proteins designated SPE-A N20D, D45N, N20D/C98S, N20D/K157E, and N20D/D45N//C98S. However, the Examiner asserts that claims encompassing compositions comprising other mutants are not enabled, in part, because Applicants have not included a SEQ ID NO in the claims. In response, the Applicants note that claims 47, 74, and 76 include SEQ ID NO's. Applicants respectfully request that this rejection be withdrawn.

To the extent that the Examiner maintains this rejection, Applicants again point out that the MPEP, at § 2164.08, indicates that "the scope of enablement must only bear a 'reasonable correlation' to the scope of the claims." As the Applicants have provided numerous working examples in addition to structural information regarding suitable mutants, the standard for enablement has been met and Applicants respectfully request that this rejection be withdrawn.

### **35 U.S.C. § 102**

Claims 31-37, 39-47, 51-55, 57-59, 61-63, 72-74, 81-83 and 85 were rejected under 35 U.S.C. 102(b) as anticipated by Weeks et al. (*Infect. Immun.*, 52(1):144-150 (1986)). Applicants respectfully traverse this rejection.

The Examiner stated that Applicant's arguments were non-persuasive because the sequence associated with SEQ ID NO: 14 was unknown. In response, Applicants point out that the specification has been amended to make the sequence associated with SEQ ID NO: 14 clear. As stated at pages 8 and 10 of the specification, SEQ ID NO: 14 is the sequence of Figure 3, (SEQ ID NO: 13) except with glutamine at position 31 designated as the first amino acid. To the extent that this rejection is still applied, the Applicants reiterate the following arguments.

Examiner asserts that since Applicants did not include a sequence in the claim language that the claimed SPE-A mutants are anticipated by all SPE-A species. Applicants note that claims 31-37, 44-47, 51-55, 57-59, 61-63, 72-74, 81-83 and 85 include SEQ ID NO's, obviating this rejection. Therefore, as Weeks does not disclose any of the mutated residues required by the current claims, it is clear that claims 31-37, 44-47, 51-55, 57-59, 61-63, 72-74, 81-83 and 85 are not anticipated by Weeks et al. Applicants respectfully request that this rejection be withdrawn.

Claims 31-37, 39-47, 51-55, 57-59, 61-63, 72-74, 81-83, and 85 were rejected under 35 U.S.C. 102(b) as anticipated by Johnson et al. (Mol. Gen. Genetics, 203:354-356 (1986)). Applicants respectfully traverse this rejection.

The Examiner stated that Applicant's arguments were non-persuasive because the sequence associated with SEQ ID NO: 14 was unknown. In response, Applicants point out that the specification has been amended to make the sequence associated with SEQ ID NO: 14 clear. As stated at pages 8 and 10 of the specification, SEQ ID NO: 14 is the sequence of Figure 3, (SEQ ID NO: 13) except with glutamine at position 31 designated as the first amino acid. To the extent that this rejection is still applied, the Applicants reiterate the following arguments.

Examiner asserts that since Applicants did not include a sequence in the claim language that the claimed SPE-A mutants are anticipated by all SPE-A species. Applicants note that claims 31-37, 44-47, 51-55, 57-59, 61-63, 72-74, 81-83, and 85 include SEQ ID NO's, obviating this rejection. Therefore, as Johnson does not disclose any of the mutated residues required by the current claims, it is clear that claims 31-37, 44-47, 51-55, 57-59, 61-63, 72-74, 81-83, and 85 are not anticipated by Johnson et al. Applicants respectfully request that this rejection be withdrawn.

### **35 U.S.C. § 112, definiteness**

Claims 31-37, 39-49, 51-55, 57-59, 61-63, 72-76, 81-83, and 85 were rejected under 35 U.S.C. § 112, second paragraph, as indefinite. Applicants respectfully traverse this rejection.

Specifically, the Examiner stated that claims 31-33, 39-40, 46-47, 51-52, 58-59, and 73-74 are rendered vague and indefinite by the use of the phrase "or substitution at more than one of these amino acids." While not conceding the correctness of Examiner's position, in the interest of advancing prosecution, Applicants have deleted this phrase from claims 31-33, 46-47, 51-52, 57-59, and 73-74 as redundant. However, it should be noted that by removing this redundant term, Applicants have not narrowed the claims. Claims 39-40 have been canceled. Applicants respectfully request that this rejection be withdrawn.

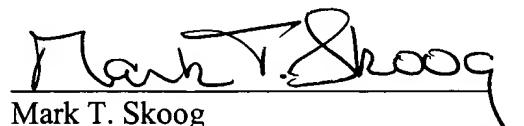
The Examiner also stated that claims 41-44 were rendered vague and indefinite by being dependent on a canceled claim. In response, claims 41-43 have been canceled without prejudice or disclaimer and claim 44 has been amended to depend on claim 36. Applicants respectfully request that this rejection be withdrawn.

### Summary

In summary, each of claims 31-37, 44-49, 51-55, 57-59, 61-63, 72-76, 81-83, and 85 are in condition for allowance and notification to that effect is solicited. The Examiner is invited to contact Applicants' undersigned representative at the telephone number listed below, if the Examiner believes that doing so will expedite prosecution of this patent application.

Respectfully submitted,  
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